CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH

SUMMARY OF TOXICOLOGY DATA
DODECYLBENZENE SULFONIC ACID and SALTS

Chemical Code # 000941, Tolerance # 50447
SB 950 # 661

Original date: March 5, 2003

I. DATA GAP STATUS

Chronic toxicity, rat:	Data gap, inadequate studies, no adverse effect indicated.
Chronic toxicity, dog:	Data gap, no study submitted
Oncogenicity, rat:	Data gap, inadequate studies, no adverse effect indicated
Oncogenicity, mouse:	Data gap, no study submitted
Reproduction, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rat:	Data gap, inadequate studies, no adverse effect indicated
Teratology, mouse:	Data gap, inadequate studies, possible adverse effect indicated
Teratology, rabbit:	Data gap, inadequate studies, no adverse effect indicated
Gene mutation:	Data gap, inadequate study, no adverse effect indicated
Chromosome effects:	Data gap, inadequate studies, no adverse effect indicated
DNA damage:	Data gap, inadequate study, no adverse effect indicated
Neurotoxicity:	Not required at this time

Toxicology one-liners are attached.
All record numbers through 133948 were examined.
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
Note: All studies are publications and without the full details needed for a detailed and critical review.
File name: T030305
Original: Kishiyama and Gee, March 5, 2003

There are 16 products currently registered in California with 12 labeled with "danger" for use as sanitizers. Three of the four remaining products contain dodecylbenzene sulfonate as an adjuvant for agricultural use.
Note:

1. The more generic term LAS (Linear Alkylbenzene Sulfonate) is used to refer to DDBSA (Dodecyl Benzene Sulfonic Acid).
2. Prior to 1965, nearly all detergent benzene alkyl sulfonate (ABS) were of the tetrapropylene sulfonate type (highly branched isomer of DDBSA), but since that time nearly all alkylbenzene sulfonate are of the LAS type for enhanced biodegradability.
3. Free acid (DDBSA is a concentrated (95%) liquid and the salts (K, Ca and Na) are 45 - 65% aqueous solutions.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

003 118382 Arthur D. Little "Environmental and human safety of major surfactants. Volume 1. Anionic surfactants. Part 1. Linear alkylbenzene sulfonates." (Arthur D. Little, VI-1 to VI-44, February, 1991) Review of published and unpublished company data with an extensive bibliography. From this list, selected publications were submitted for addressing the requirements of SB950. This Summary of Toxicology Data contains the review of those most pertinent. In a number of instances, a full worksheet has not been prepared but a summary has been included here. (Gee, 2/27/03)

003 126934 Swisher, R. D. "Exposure levels and oral toxicity of surfactants." (Monsanto, publ. in *Arch. Environ. Health* 17: 232 - 246 (1968)) Review article of publications up to 1966. No worksheet. (Gee, 2/24/03).

CHRONIC TOXICITY, RAT

003 126874 Buehler, E. V., E. A. Newmann, and W. R. King. "Two-Year Feeding and Reproduction Study in Rats with Linear Alkybenzene Sulfonate (LAS)." (The Proctor & Gamble Co., Miami Valley Laboratories, publ. in *Toxicology and Applied Pharmacology* 18: 83-91 (1971)). LAS, sodium salt (41.9% active, anhydrous basis of 98.1%), was mixed in the diet at concentrations of 0, 0.02 (20 mg/kg early in growth phase), 0.1 and 0.5% and fed to 50 rats/sex/group. Groups of 5/sex were sacrificed at 8 and 15 months. Hematology parameters were examined periodically. No clinical chemistry, urinalysis or ophthalmologic exam were included in the protocol. Groups of 20 per sex per group were removed after 84 days on the test diets for a reproduction study (see that worksheet) and returned to the 2-year study after completion of the F1b litters. There was no affect of treatment on liver or kidney weights, or on body weights. Although no data were presented, the text states that there were no treatment- related effects on histopathology, although animals showed a "high incidence" of intercurrent diseases. Apparent NOEL > 5000 ppm (0.5% of diet). UNACCEPTABLE (insufficient data for evaluation). Not upgradeable. (Kishiyama and Gee, 2/10/03)

007 133918 Duplicate of 003 126874.

007 133917 Paynter, O. E. and R. J. Weir, Jr. “Chronic Toxicity of Santomerse No. 3 from

Olefin (Dodecyl Benzene Sodium Sulfonate)." (Hazleton Laboratories, publ. in *Toxicology and Applied Pharmacology* 2: 641 - 648 (1960)). Santomerse No. 3 from Olefin (97-98.5% pure, 90% C_{11} to C_{13}) was admixed with the feed at concentrations of 0, 200, 1000 and 2000 ppm and fed to 20 male rats/group (Carworth Farms strain) and at 0 and 1000 ppm and fed to 20 female rats/group. Treatment was for 104 weeks. Dose selection was based on a range-finding study. Limited hematology was conducted but no clinical chemistry, urinalysis or ophthalmology was included. The list of tissues for histopathology was limited and only 3/sex/group were examined. No treatment- related effects were reported as being found, therefore the nominal NOEL may be > 2000 ppm (M). Limited summary data were included in the publication. UNACCEPTABLE. Not upgradeable (major variances and insufficient information). (Kishiyama and Gee, 2/20/03)

003 126924 Incomplete copy of 007 133917.

007 133914 Layton, D. W., B. J. Mallon, D. H. Rosenblatt and M. J. Small "Deriving allowable daily intakes for systemic toxicants lacking chronic toxicity data." (Lawrence Livermore National Laboratory and U. S. Army Medical Bioengineering Research and Development Laboratory, publ. in *Regulatory Toxicol. Pharmacol.* 7: 96 - 112 (1987)) The authors reviewed published data regarding LD_{50} values and NOELs from longer term studies (not clearly defined) for small mammals. Using these ratios for a large number of chemicals, including some pesticides, they came up with a recommendation to use a factor in the range of 5×10^{-6} to 1×10^{-5} to convert a LD_{50} to an acceptable daily intake (ADI). One of the chemicals included in the tables was sodium dodecylbenzene sulfonate with an LD_{50} of 1260 mg/kg for rat and 2000 mg/kg for mouse and a NOEL for both species of 150 mg/kg/day - the rat value was from Frawley, J. P., *Food Cosmet. Toxicol.* 5: 293 - 308 (1967), with no further information. Supplemental publication. No worksheet. (Gee, 2/25/03).

SUBCHRONIC, RAT

003 126900 Kay, J. H., F. E. Kohn and J. C. Calandra "Subacute oral toxicity of a biodegradable, linear alkylbenzene sulfonate." (IBT, publ. in *Toxicol. Appl. Pharmacol.* 7: 812 - 818 (1965) Sodium alkylbenzene sulfonate, 87.9%, was fed in the diet at levels of 0, 0.02, 0.1 or 0.5 % [250 mg/kg] to 10/sex Sprague-Dawley rats for 90 days. There were no findings reported for body weight, food consumption, hematology, organ weight or microscopic examination. The status of this study in terms of audit is unknown, therefore, considered UNACCEPTABLE and not upgradeable. No worksheet. No adverse effect. (Gee, 2/14/03),

007 133911 Duplicate of 003 126900.

003 126909 Mathur, A. K., B. N. Gupta, A. Singh and R. Shanker "Toxicological evaluation of a synthetic detergent after repeated oral ingestion in rats." (Industrial Toxicology Research Centre, Lucknow, publ. in *Bio. Mem.* 12: 187 - 191 (1986)) Groups of nine female albino rats were given doses of linear alkylbenzene sulfonate (no purity or description) of 0 (water), 50, 100 or 250 mg/kg daily by gavage, 5 days per week for 10 weeks. At termination, animals were fasted for 24 hours before sacrifice and liver, kidney, heart and intestines were weighed. These organs were prepared for histology. The liver and kidneys were evaluated for certain enzymes. Weight gain was lower in treated animals than controls, especially at 100 and 250 mg/kg. Liver and kidneys showed changes in histology and some enzymes were increased or decreased. Apparent NOEL = 50 mg/kg/day. Supplemental study. No worksheet. (Gee, 2/18/03).

007 133912 Duplicate of 003 126909

007 133837 Oser, B. L. and K. Morgareidge "Toxicologic studies with branched and linear alkyl benzene sulfonates in rats." (Food and Drug Research Laboratories, publ. in *Toxicology and Applied Pharmacology* 7: 819 - 825 (1965)) LAS (39.5% with 50.9% water and 8.8% sodium sulfate) was fed in the diet to yield doses of 0, 0.05 and 0.25 g/kg/day [38% of the LD50 by these authors] with 15/sex/group FDRL (Wistar derived) rats for 12 weeks. Doses were in terms of % active ingredient and the ppm in the diet adjusted biweekly to maintain the doses. At week 11, this was equivalent to 1000 and 5000 ppm. Limited hematology, clinical chemistry and urinalysis parameters were evaluated. The liver, kidneys, spleen, heart, adrenals, pituitary and cecum were weighed. These plus additional tissues were examined microscopically for 5/sex of controls and 0.25 g/kg groups. Body weight gain and food consumption were comparable with controls. Liver weight/body weight was significantly increased at the high dose in females. The others were comparable. No other gross or histological findings related to treatment were reported. UNACCEPTABLE (inadequate parameters evaluated for hematology, urinalysis, clinical chemistry; no ophthalmology; not all animals for histology. Not upgradeable. No adverse effect. NOEL not clearly determined. No worksheet. (Gee, 2/21/03)

003 126929 Incomplete version of the publication in 133837.

007 133913 Scailteur, V., J. K. Maurer, A. P. Walker and G. Calvin "Subchronic oral toxicity testing in rats with a liquid hand-dishwashing detergent containing anionic surfactants." (Proctor and Gamble, others, publ. in *Food Chem. Toxicol.* 24: 175 - 181 (1986)) LAS was one of several surfactant in a mixture tested at 0.025, 0.25 or 2.5% (w/w) with Sprague-Dawley rats, 20/sex/group. Diets were fed for 13 weeks. Relative liver weight was increased at 2.5% of the mixture. Not reviewed because test material was a mixture. No worksheet. (Gee, 2/21/03)

003 126930 Duplicate of 133913 with pages out of order.

003 No record number. Publication cited but not submitted. Yoneyama, M., T. Fujii, M. Ikawa, H. Shiba, Y. Sakamoto, N. Yano, H. Kobayashi, H. Ichikawa and K. Hiraga "Studies on toxicity of synthetic detergents. II. Subacute toxicity of linear and branched alkyl benzene sulfonate in rats." (publ. in *Tokyo Toritsu Eisei Kenkyusho Nempo* 24: 409 - 440 (1973)) Wistar rats (number and sex not stated) were fed DDBSA at 0.07 (40 mg/kg/day), 0.2%, 0.6% (340 mg/kg/day) and 1.8% (1000 mg/kg/day) for 6 months. At the high dose, tissue damage was noted in the cecum and liver with some kidney pathology. The summary states that the NOEL was 700 ppm with a LOEL of 0.2% (2000 ppm) based on kidney or liver - not clear. No worksheet. Publication not on file. (Gee, 2/27/03)

SUBCHRONIC, MONKEY

003 126877 Coate, W. B., W. M. Busey, W. H. Schoenfisch, N. M. Brown and E. A. Newmann "Respiratory toxicity of enzyme detergent dust." (Hazleton Laboratories America, publ. in *Toxicology and Applied Pharmacology* 45: 477 - 496 (1978)) Cynomolgus monkeys were exposed for 6 hours/day, 5 days/week for 6 months to synthetic laundry detergent, enzymes (2:1 mix of Alcalase (a subtilopeptidase A) and Milezyme 8X (a mixture of subtilopeptidase B, α-amylase and a neutral protease)) and mixtures of these. The detergent used contained 13% C_{12} linear alkylbenzene sulfonate plus sodium tripolyphosphate (39%), sodium sulfate (40%), sodium silicate (7%) and water (1%). The detergent was milled so that the particle size was 90% < 5 μm.

There were 5 male and 4 female monkeys in each of 12 groups. Dust concentrations in mg/m^3 were: enzyme mix, 0, 0.001, 0.01, 0.1 or 1; detergent mix, 0, 1 10 or 100 (0.013 mg/L, DDBSA). These were tested in various combinations. Exposure was stopped at 17 weeks for those exposed to 100 mg/m^3 plus 0.1 or 1 mg/m^3 enzyme due to loss of animals. Some animals were held for a recovery period. Groups receiving 100 mg/m^3 of detergent had some mortality with lung pathology noted. Hematology, clinical chemistry and urinalysis parameters were measured pretest, monthly and at termination. Most guideline parameters were included. Pulmonary function tests were also performed on the same schedule. Serum samples were taken at monthly intervals (see also record 126876 below). Most required tissues were saved with special emphasis on lung sections. The following variables were comparable to controls: pulmonary function tests, hematology, clinical chemistry, urinalysis, chest x-rays, intradermal and prick tests. Clinical signs of coughing, labored breathing or decreased activity were noted during exposure in groups exposed to 10 or 100 mg/m^3 of detergent. Those exposed to 1 mg/m^3 LAS plus 0.001 to 0.1 mg/m^3 of enzyme mix did not show signs of gross respiratory effects. Lower weight gain was related to enzyme concentration during the exposure period (no data), with recovery. Animals at 100 mg/m^3 of detergent lost weight during exposure period. Lung histopathology (chronic bronchiolitis, fibrosis, others) was seen in animals exposed to 10 or 100 mg/m^3 of detergent and to 1 mg/m^3 enzyme plus 1 mg/m^3 detergent. No findings were seen in the upper respiratory tract. No effects were seen at 1 mg/m^3 detergent plus enzyme up to 0.1 mg/m^3. Not designed to determine the NOEL for each alone. Supplemental study. No worksheet. (Gee, 2/11/03)

007 133838 duplicate of 003 126877.

CHRONIC TOXICITY, DOG

No Study Submitted

ONCOGENICITY, RAT

008 133928 Takahashi, M. and H. Sato. "Effect of 4-Nitroquinoline 1-Oxide with Alkylbenzenesulfonate on Gastric Carcinogenesis in Rats." (Nagoya City University, publ. in *GANN Monographs*, No. 8: 241 - 246 (1969)). 4-Nitroquinoline 1-Oxide (1 mg/rat in 20% ethanol) alone or combined with alkylbenzene sulfonate (8%) (53% dodecyl, alkyl with range of C9 - C15) was administered via gavage, 2-3 times/week for 18 weeks to male Moriyama and Wistar rats. Group 1 (combination) had 79 rats, group 2 had 17 rats, which were fasted for 12 hours before being given the combination, group 3 had 37 given 4-NQO alone and group 4 with 28 rats was given alkylbenzene sulfonate alone. No tumors were found with alkylbenzene sulfonate alone. The incidence of adenocarcinoma of the glandular stomach (5/59 versus 0 with 4-NQO alone) and of malignant papillomas of the forestomach (32/59 versus 7/33) increased with the combination. Supplemental study. (Kishiyama and Gee, 2/24/03).

003 126941 Same study as 008 133928.

003 126935 Takahashi, M. "Effect of Alkylbenzenesulfonate as a Vehicle for 4-Nitroquinoline 1-Oxide on Gastric Carcinogenesis in Rats." (Nagoya City University, publ. in *GANN* 61: 27 - 33 (1970)). 4-Nitroquinoline 1-Oxide (1 mg) was dissolved in 1 ml of 20% ethanol containing 8% alkylbenzensulfonate (no purity or description) and administered via gavage to 37 male Moriyama strain rats 2-3 times/week for 18 weeks. Other groups of 13 male

rats were given either 4-NQO in ethanol or 8% ABS in 20% ethanol. Survival beyond the 18 weeks was 15/37, 9/13 and 10/13. The increase in tumor incidence in the stomach was considered due to the presence of alkylbenzenesulfonate when used in the vehicle for 4-Nitroquinoline 1-Oxide. No tumors occurred with ABS alone. With 4-NQO alone, there were 9 benign papillomas of the forestomach. UNACCEPTABLE, supplemental study. (Kishiyama and Gee, 2/24/03).

008 133929 Same study as 003 126935.

008 133931 Takahashi, M., S. Fukushima and M. Hananouchi "Induction of undifferentiated adenocarcinoma in the stomach of rats by N-methyl-N'-nitro-N-nitrosoguanidine with various kinds of surfactants." (Nagoya City University, publ. in *GANN Monograph on Cancer Research* 17: 255 - 267 (1975)). Male Wistar rats were given MNNG at 100 mg/liter alone or with a surfactant. Fifteen and 10 rats per group were given 0.1% "hard type" alkylbenzenesulfonate (branched alkyl chain) or "soft type" alkylbenzenesufonate (linear alkyl chain) for 63 weeks. Rats were then given tap water until termination. Rats surviving more than 18 weeks from the beginning of the experiment were considered effective. The incidence for adenocarcinomas in the glandular stomach were 4/10 (2 well-differentiated and 2 undifferentiated) with linear alkyl benzenesulfonate plus MNNG and 8/13 (62%, all well-differentiated) with MNNG alone. Supplemental study. No worksheet. (Gee, 2/24/03).

003 126937 Same study included in 008 133931.

008 133930 Takahashi, M., S. Fukushima, and H. Sato. “Carcinogenic Effect of N-Methyl-N’-Nitro-N-Nitrosoguanidine with Various Kinds of Surfactant in the Glandular Stomach of Rats.” (Nagoya City University, publ. in *GANN* 64: 211 - 218 (June, 1973)). N-Methyl-N’-Nitro-N-Nitrosoguanidine was combined with the following surfactants: Tween 60, Nonipol, Alkylbenzenesulfonate (hard type, branched alkyl chain), or Alkylbenzenesulfonate (soft type, linear alkyl chain) and administered in the drinking water of male Wistar rats. The incidence of adenocarcinoma in the glandular stomach was reported with MNNG when in combination with surfactants and alone. The data are the same as in 008 133931. Supplemental study. (Kishiyama and Gee, 2/24/03).

003 126939 Same study as 008 133930.

ONCOGENICITY, MOUSE

No Study Submitted

Proctor and Gamble, unpublished, no date. Summarized in Arthur D. Little, 1991 as follows: Swiss ICR mice were given dermal applications of detergent containing 15.6% DDBSA and 18.6% tallow alkyl ethoxylate sulfate three times weekly for 18 months at aqueous concentrations of 0.1, 1.0 or 10 %. Summary states there were no carcinogenic response for skin or systemically. At 10%, acanthosis and/or hyperkeratosis of the treated skin were noted. (Gee, 2/27/03)

REPRODUCTION, RAT

003 126874 Buehler, E. V., E. A. Newmann, and W. R. King. "Two-Year Feeding and Reproduction Study in Rats with Linear Alkybenzene Sulfonate (LAS)." (The Proctor & Gamble

Co., Miami Valley Laboratories, publ. in *Toxicology and Applied Pharmacology* 18. 83-91 (1971)). LAS (sodium salt, 41.9% acitve, 98.1% anhydrous) was mixed in the diet at concentrations of 0, 0.02, 0.1 and 0.5% and fed to 50 rats/sex/group. For the reproduction segment, 20/sex/group were removed from the 2-year study after 84 days on diets to form the P generation. The first litters (F1a and F2a) were sacrificed on day 21. P adults were remated for the F1b and F2b litters. Necropsy was performed on 5/sex/group of the F1b and F2b adults and the F3a weanlings. From the text and the limited summary data presented, there were no treatment-related effects on reproductive parameters (litter size, pup weight, histology) or other endpoints. Apparent NOEL > 0.5% of the diet. Unacceptable (insufficient data, no analysis of diets, no individual data, limited summary data - see worksheet). Not upgradeable. (Kishiyama and Gee, 2/10/03)

007 133918 Same study as 126874.

TERATOLOGY, RAT

003 126889 Daly, I. W., R. E. Schroeder, and J. C. Killeen. "A Teratology Study of Topically applied Linear Alkybenzene Sulphonate in Rats." (Bio/dynamics, Inc. and Diamond Shamrock, publ. in *Food Cosmet. Toxicol.* 18: 55 - 58 (1980)). Linear Alkybenzene Sulphonate (LAS, 20.5% with 78.7% water) was administered dermally at concentrations of 0, 0.05, 0.1 and 0.5%, continuously, and at 1.0, 5.0, and 20% ai for 30 minutes, then removed with tap water. These were equivalent to doses of 1, 2, 10, 20, 100 and 400 mg/kg with increasing concentrations. Doses were applied in 0.5 ml, spread with a gloved finger, and were not covered. Groups contained at least 20 mated Wistar female rats with dosing on gestation days 0 through 20. Fetuses were evaluated on day 21. No developmental effects reported. Maternal body weight was slightly lower at day 21 at 400 mg/kg. Dermal effects were noted at 20 mg/kg and higher, consisting of discoloration, erythema, slight thickening and fissuring with signs seen primarily in the first 6 days with lessening or disappearing as dosing continued. Apparent maternal NOEL = 10 mg/kg (0.5%) for dermal effects, 100 mg/kg for systemic effects (body weight). No developmental findings - NOEL = 400 mg/kg. UNACCEPTABLE (insufficient information). Upgrade questionable. (Kishiyama and Gee, 2/11/03).

008 133940 Nolen, G. A., L. W. Klusman, L. F. Patrick, and R. G. Geil. "Teratology Studies of a Mixture of Tallow Alkyl Ethoxylate and Linear Alkylbenzene Sulfonate in Rats and Rabbits." (Proctor and Gamble Company, Miami Valley Laboratories, publ. in *Toxicology* 4: 231-243 (1975)). A mixture of 55% tallow alkyl ethoxylate and 45% linear alkylbenzene sulfonate (purities not stated) was fed continuously to 25/sex for 2 generations (3 matings per generation) at concentrations of 0.1, 0.5 or 1.0% to Sprague-Dawley (Charles River) rats or to females for days 6 through 15 of gestation. The first two matings proceeded to natural births and the third mating fetuses (F1c and F2c) were used for developmental toxicity. The F1b became the parental animals for the F2 litters. For the teratology portion, approximately half the dams were sacrificed on day 13 and the remainder on day 21. Fetuses were examined for soft tissue and skeletal defects. There were no treatment-related effects on reproductive parameters and no developmental effects reported. UNACCEPTABLE, supplemental (use of a mixture of compounds, other deficiencies - see worksheet.) Not upgradeable. (Kishiyama and Gee, 2/19/03).

003 126918 same publication as 008 133940.

003 126920 Palmer, A. K., M. A. Readshaw and A. M. Neuff. "Assessment of the Teratogenic

potential of Surfactants-Part I - LAS, AS and CLD." (Huntingdon Research Centre, publ. in. *Toxicology* 3: 91 - 106 (1975)). Linear Alkylbenzene Sulfonate (LAS, no purity given [may be technical]) was administered via oral gavage at doses of 0 (water), 0.2, 2.0, 300 or 600 mg/kg/day during gestation days 6-15 for CD rats and CD-1 mice and gestation days 6-18 for New Zealand White rabbits. There were 20 mated mice and rats per group and 13 rabbits. MICE: Mortality at 300 mg/kg was 7/20 with total litter losses of 4; at 600 mg/kg, 18 died and there were no litters with viable young, with 1 total litter loss. Of those surviving and producing viable fetuses, there were no differences in litter size, fetal weight or fetal findings, compared with controls. RATS: One dam died at 600 mg/kg and there was one total litter loss at 0.2 mg/kg. There were no differences in litter size, fetal weight or fetal findings. At termination, there were 15, 11, 18, 16 and 16 viable litters with increasing dose. RABBITS: Mortality for rabbits was 2 (one intubation error), 0, 1, 11 and 13 with increasing dose. Viable litters at termination were 9, 12, 11, 0 and 0 with increasing dose. Of the viable litters, there were no treatment- related findings. LAS at 300 and 600 mg/kg/day was maternally toxic to mice and rabbits with signs of anorexia, weight retardation, cachexia, and death and, consequently, fetal loss and at 600 to rats (weight gain, slight reaction). No data for clinical sign incidences were included. Similar data were presented for AS (alcohol sulfonate) and CLD (commercial liquid detergent containing 17% LAS and 7% sodium dodecyl ethoxy sulfate). Maternal NOEL not determined due to spacing of doses. No evidence of developmental toxicity without maternal toxicity. UNACCEPTABLE (inadequate number of fetuses available for assessment, dose selection not intended for a dose response but for maximum likely human intake and for maternal toxicity - see worksheet). Not upgradeable as a FIFRA study. (Kishiyama and Gee, 2/20/03).

008 133943 Duplicate of 126920.

008 133944 Palmer, A. K., M. A. Readshaw and A. M. Neuff. "Assessment of the Teratogenic Potential of Surfactants-Part III - Dermal Application of LAS and Soap." (Huntingdon Research Centre, publ. in *Toxicology* 4:171 - 181 (1975)). Linear Alkylbenzene Sulfonate (LAS, no purity stated) was administered dermally at concentrations of 0 (water), 0.03, 0.3 and 3% (w/v) during gestation days 2-15 for CD rats, 2 - 13 for CD-1 mice and days 1-16 for New Zealand White rabbits. The test solutions were applied to the following areas: 2 x 3 cm, mice; 4 x 4 cm, rats and 12 x 20 cm for rabbits, using 0.5 ml for rats and mice and 10 ml for rabbits. The dosing material was not occluded or the site washed. The doses were, in mg/kg/day, for mice, 5, 50 or 500; for rats, 0.6, 6 or 60; for rabbits, 0.9, 9 or 90 mg/kg/day. High dose (3%) treated mice and rabbit groups showed local skin reaction of severe irritation, weight loss and fewer litters with viable young. Mortality did not show a dose relationship in any species. Because the sites were not washed, some skin effects may have been obscured by the accumulation of the test article. MICE: Total litter loss was 2, 0, 4 and 5 with increasing dose. Dams with viable young were 14, 15, 14 and 1 with 3, 4, 2 and 14 not pregnant (dosing started day 2 prior to implantation). For those with live fetuses, the mean litter size and fetal weights were not affected. Nominal maternal/developmental NOEL = 0.03% (5 mg/kg/day). RAT: Rats were the least affected of the three species. Only mild or moderate skin sensitivity was noted at 3%. There were no effects on fetuses/litters. Nominal maternal/developmental NOEL = 3% (60 mg/kg/day). RABBITS: Severe local reaction (erythema and edema with peak days 6-7 progressing to cracking and bleeding) was seen at 3% and mild/moderate at 0.3% with "marked loss" in weight at 3 % (no data). Total litter loss was 0, 0, 0 and 2 with viable litters of 11, 12, 12 and 9. Litter size was 9.7, 8.1, 10.0 and 7.3 with increasing dose - not statistically significant. Nominal maternal/developmental NOEL = 0.3% (9 mg/kg/day). For all three species, no developmental abnormalities related to treatment were reported. No adverse developmental effect. UNACCEPTABLE (major deficiencies and insufficient information - see worksheet). Not

upgradeable. (Kishiyama and Gee, 2/20/03).

003 126922 Same study as 133944 above.

TERATOLOGY, RABBIT

008 133940A Nolen, G. A., L. W. Klusman, L. F. Patrick, and R. G. Geil. "Teratology Studies of a Mixture of Tallow Alkyl Ethoxylate and Linear Alkylbenzene Sulfonate in Rats and Rabbits." (Proctor and Gamble Company, Miami Valley Laboratories, publ. in *Toxicology* 4: 231 - 243 (1975)). A mixture of 55% tallow alkyl ethoxylate and 45% linear alkylbenzene sulfonate (purities not stated) was administered via gavage at doses of 0, 50, 100 or 300 mg/kg during gestation days 2 - 16 to 25 artificially inseminated New Zealand females/group. No treatment related effects were reported. Nominal Maternal NOEL = >300 mg/kg and Developmental NOEL = >300 mg/kg for the mixture. UNACCEPTABLE, supplemental study (mixture of chemicals, other deficiencies - see worksheet). Not upgradeable. (Kishiyama and Gee, 2/19/03).

003 126918 Duplicate of 008 133940A above.

003 126920 Palmer, A. K., M. A. Readshaw and A. M. Neuff. "Assessment of the Teratogenic potential of Surfactants-Part I - LAS, AS and CLD." (Huntingdon Research Centre, publ. in. *Toxicology* 3: 91 - 106 (1975)). Linear Alkylbenzene Sulfonate (LAS, no purity given [may be technical]) was administered via oral gavage at doses of 0 (water), 0.2, 2.0, 300 or 600 mg/kg/day during gestation days 6-15 for CD rats and CD-1 mice and gestation days 6-18 for New Zealand White rabbits. There were 20 mated mice and rats per group and 13 rabbits. MICE: Mortality at 300 mg/kg was 7/20 with total litter losses of 4; at 600 mg/kg, 18 died and there were no litters with viable young, with 1 total litter loss. Of those surviving and producing viable fetuses, there were no differences in litter size, fetal weight or fetal findings, compared with controls. RATS: One dam died at 600 mg/kg and there was one total litter loss at 0.2 mg/kg. There were no differences in litter size, fetal weight or fetal findings. At termination, there were 15, 11, 18, 16 and 16 viable litters with increasing dose. RABBITS: Mortality for rabbits was 2 (one intubation error), 0, 1, 11 and 13 with increasing dose. Viable litters at termination were 9, 12, 11, 0 and 0 with increasing dose. Of the viable litters, there were no treatment- related findings. LAS at 300 and 600 mg/kg/day was maternally toxic to mice and rabbits with signs of anorexia, weight retardation, cachexia, and death and, consequently, fetal loss and at 600 to rats (weight gain, slight reaction). No data for clinical sign incidences were included. Similar data were presented for AS (alcohol sulfonate) and CLD (commercial liquid detergent containing 17% LAS and 7% sodium dodecyl ethoxy sulfate). Maternal NOEL not determined due to spacing of doses. No evidence of developmental toxicity without maternal toxicity. UNACCEPTABLE (inadequate number of fetuses available for assessment, dose selection not intended for a dose response but for maximum likely human intake and for maternal toxicity - see worksheet). Not upgradeable as a FIFRA study. (Kishiyama and Gee, 2/20/03).

008 133943 Duplicate of 126920

008 133944 Palmer, A. K., M. A. Readshaw and A. M. Neuff. "Assessment of the Teratogenic Potential of Surfactants-Part III - Dermal Application of LAS and Soap." (Huntingdon Research Centre, publ. in *Toxicology* 4:171 - 181 (1975)). Linear Alkylbenzene Sulfonate (LAS, no purity stated) was administered dermally at concentrations of 0 (water), 0.03, 0.3 and 3% (w/v) during gestation days 2-15 for CD rats, 2 - 13 for CD-1 mice and days 1-16 for New Zealand

White rabbits. The test solutions were applied to the following areas: 2 x 3 cm, mice; 4 x 4 cm, rats and 12 x 20 cm for rabbits, using 0.5 ml for rats and mice and 10 ml for rabbits. The dosing material was not occluded or the site washed. The doses were, in mg/kg/day, for mice, 5, 50 or 500; for rats, 0.6, 6 or 60; for rabbits, 0.9, 9 or 90 mg/kg/day. High dose (3%) treated mice and rabbit groups showed local skin reaction of severe irritation, weight loss and fewer litters with viable young. Mortality did not show a dose relationship in any species. Because the sites were not washed, some skin effects may have been obscured by the accumulation of the test article. MICE: Total litter loss was 2, 0, 4 and 5 with increasing dose. Dams with viable young were 14, 15, 14 and 1 with 3, 4, 2 and 14 not pregnant (dosing started day 2 prior to implantation). For those with live fetuses, the mean litter size and fetal weights were not affected. Nominal maternal/developmental NOEL = 0.03% (5 mg/kg/day). RAT: Rats were the least affected of the three species. Only mild or moderate skin sensitivity was noted at 3%. There were no effects on fetuses/litters. Nominal maternal/developmental NOEL = 3% (60 mg/kg/day). RABBITS: Severe local reaction (erythema and edema with peak days 6-7 progressing to cracking and bleeding) was seen at 3% and mild/moderate at 0.3% with "marked loss" in weight at 3 % (no data). Total litter loss was 0, 0, 0 and 2 with viable litters of 11, 12, 12 and 9. Litter size was 9.7, 8.1, 10.0 and 7.3 with increasing dose - not statistically significant. Nominal maternal/developmental NOEL = 0.3% (9 mg/kg/day). For all three species, no developmental abnormalities related to treatment were reported. No adverse developmental effect. UNACCEPTABLE (major deficiencies and insufficient information - see worksheet). Not upgradeable. (Kishiyama and Gee, 2/20/03).

003 126922 Duplicate.

TERATOLOGY, MOUSE

003 126905 Koizumi, N., R. Ninomiya, Y. Inoue, T. Tsukamoto, M. Fujii, and Y. Yamamoto. "Implantation Disturbance Studies with Linear Alkylbenzene Sulphonate in Mice." (Hyogo College of Medicine and Food Chemistry Division, Ministry of Health and Welfare, Japan, Publ. in *Archives Environmental Contamination and Toxicology* 14: 73 - 81 (1985)). Linear alkylbenzene sulfonate (LAS, 20% w/w) was administered to ICR female mice in several experiments. In experiment 1, for preimplantation lose, doses were 0, 14, 70 or 350 mg/kg by oral gavage, either on day 3 as a single dose or on days 1 - 3 of gestation, with 30+ per group. In experiment 2, for distribution in tissues, a dose of 350 mg/kg was given on day 3 and the animals (10) were sacrificed at 4 or 8 hours. Distribution was determined by HPLC quantitation. In experiment three, mice were given 2 mg/mouse on day 3 (approximately 70 mg/kg) and sacrificed on day 18 for analysis of polychromatic erythrocytes or were given subcutaneous injections of 0, 1, 2, and 10 mg/mouse on day 17. Bone marrow was evaluated 24 hours later for effects on maternal bone marrow and fetal liver and blood cells. No treatment related effects were reported on implantation, live fetuses per litter or fetal weight in experiment 1. In mice treated on day 3, distribution at 4 hours was primarily in the stomach/intestine, liver and blood. At 8 hours, the amount in the liver had increased over 4 hours, material was found in the kidney (urinary excretion), blood level increased and stomach/intestine decreased. There was no increase in micronucleated polychromatic erythrocytes by either dosing regimen - oral on day 3 (2 mg/mouse) or subcutaneous on day 17 of gestation. No adverse effects. Supplemental study. (Kishiyama and Gee, 2/14/03).

003 126908 Masuda, F., K. Okamoto and K. Inoue "Effects of linear alkylbenzene sulfonate applied dermally to pregnant mice on the development of their fetuses." (Kao Soap, Japan, publ.

in *Shokuhin Eiseigaku Zasshi* 15: 349 - 355 (1974)) In Japanese with English abstract and tables. ICR-JCL and ddY strains of mice were used. LAS was given in 0.5 ml/mouse at concentrations of 0.85, 1.7, 2.55 and 3.4%, days 1 - 13 of gestation with ICR-JCL mice [estimated as 140, 280, 425 and 560 mg/kg/day] and at 0.017, 0.17 and 1.7% with ddY mice [estimated as 2.8, 28 and 280 mg/kg/day], days 2 - 14 of gestation. No effects on body weight or organ weights. Pregnancy rate was reduced at 3.4% (33.3%* or 10/30 versus 69% in water controls) in the presence of considerable skin irritation at the application site. Non dose-related lower fetal weights were noted with ICR-JCL mice. Retarded ossification was noted at 2.55 and 3.4% LAS compared with controls. No conclusive evidence of teratogenic effects were noted, according to the abstract and available data (summary only). No worksheet. (Gee, 2/18/03)

008 133933 Same publication as 126908.

003 126920 Palmer, A. K., M. A. Readshaw and A. M. Neuff. "Assessment of the Teratogenic potential of Surfactants-Part I - LAS, AS and CLD." (Huntingdon Research Centre, publ. in. *Toxicology* 3: 91 - 106 (1975)). Linear Alkylbenzene Sulfonate (LAS, no purity given [may be technical]) was administered via oral gavage at doses of 0 (water), 0.2, 2.0, 300 or 600 mg/kg/day during gestation days 6-15 for CD rats and CD-1 mice and gestation days 6-18 for New Zealand White rabbits. There were 20 mated mice and rats per group and 13 rabbits. MICE: Mortality at 300 mg/kg was 7/20 with total litter losses of 4; at 600 mg/kg, 18 died and there were no litters with viable young, with 1 total litter loss. Of those surviving and producing viable fetuses, there were no differences in litter size, fetal weight or fetal findings, compared with controls. RATS: One dam died at 600 mg/kg and there was one total litter loss at 0.2 mg/kg. There were no differences in litter size, fetal weight or fetal findings. At termination, there were 15, 11, 18, 16 and 16 viable litters with increasing dose. RABBITS: Mortality for rabbits was 2 (one intubation error), 0, 1, 11 and 13 with increasing dose. Viable litters at termination were 9, 12, 11, 0 and 0 with increasing dose. Of the viable litters, there were no treatment- related findings. LAS at 300 and 600 mg/kg/day was maternally toxic to mice and rabbits with signs of anorexia, weight retardation, cachexia, and death and, consequently, fetal loss and at 600 to rats (weight gain, slight reaction). No data for clinical sign incidences were included. Similar data were presented for AS (alcohol sulfonate) and CLD (commercial liquid detergent containing 17% LAS and 7% sodium dodecyl ethoxy sulfate). Maternal NOEL not determined due to spacing of doses. No evidence of developmental toxicity without maternal toxicity. UNACCEPTABLE (inadequate number of fetuses available for assessment, dose selection not intended for a dose response but for maximum likely human intake and for maternal toxicity - see worksheet). Not upgradeable as a FIFRA study. (Kishiyama and Gee, 2/20/03).

008 133943 Same as 126920.

008 133944 Palmer, A. K., M. A. Readshaw and A. M. Neuff. "Assessment of the Teratogenic Potential of Surfactants-Part III - Dermal Application of LAS and Soap." (Huntingdon Research Centre, publ. in *Toxicology* 4:171 - 181 (1975)). Linear Alkylbenzene Sulfonate (LAS, no purity stated) was administered dermally at concentrations of 0 (water), 0.03, 0.3 and 3% (w/v) during gestation days 2-15 for CD rats, 2 - 13 for CD-1 mice and days 1-16 for New Zealand White rabbits. The test solutions were applied to the following areas: 2 x 3 cm, mice; 4 x 4 cm, rats and 12 x 20 cm for rabbits, using 0.5 ml for rats and mice and 10 ml for rabbits. The dosing material was not occluded or the site washed. The doses were, in mg/kg/day, for mice, 5, 50 or 500; for rats, 0.6, 6 or 60; for rabbits, 0.9, 9 or 90 mg/kg/day. High dose (3%) treated mice and rabbit groups showed local skin reaction of severe irritation, weight loss and fewer litters with viable young. Mortality did not show a dose relationship in any species. Because the sites were

not washed, some skin effects may have been obscured by the accumulation of the test article. MICE: Total litter loss was 2, 0, 4 and 5 with increasing dose. Dams with viable young were 14, 15, 14 and 1 with 3, 4, 2 and 14 not pregnant (dosing started day 2 prior to implantation). For those with live fetuses, the mean litter size and fetal weights were not affected. Nominal maternal/developmental NOEL = 0.03% (5 mg/kg/day). RAT: Rats were the least affected of the three species. Only mild or moderate skin sensitivity was noted at 3%. There were no effects on fetuses/litters. Nominal maternal/developmental NOEL = 3% (60 mg/kg/day). RABBITS: Severe local reaction (erythema and edema with peak days 6-7 progressing to cracking and bleeding) was seen at 3% and mild/moderate at 0.3% with "marked loss" in weight at 3 % (no data). Total litter loss was 0, 0, 0 and 2 with viable litters of 11, 12, 12 and 9. Litter size was 9.7, 8.1, 10.0 and 7.3 with increasing dose - not statistically significant. Nominal maternal/developmental NOEL = 0.3% (9 mg/kg/day). For all three species, no developmental abnormalities related to treatment were reported. No adverse developmental effect. UNACCEPTABLE (major deficiencies and insufficient information - see worksheet). Not upgradeable. (Kishiyama and Gee, 2/20/03).

003 126922 Same study as 008 133944.

003 126926 Nomura, T., S. Hata, K. Shibata, and T. Kusafuka. "Killing of Preimplantation Mouse Embryos by Main Ingredients of Cleansers AS and LAS." (Dept. of Fundamental Radiology and Institute for Cancer Research, Osaka Univ., publ. in *Mutation Research* 190: 25 - 29 (1987)). Linear Alkylbenzene Sulfonate (LAS, no purity stated) at 20% aqueous solution and Alcohol Sulfate (AS) at 2 - 20% were administered dermally to pregnant JCL:ICR mice at 10:00 and 17:00 hours on gestation days 0, 1, and 2. Volume applied was 0.1 ml to a 2x3 cm area from which the hair had been "plucked" on day 0, following determination of mating. Mice were sacrificed on day 3 (10:00 am). Embryos were flushed from the uterus and oviducts. After microscopic examination, embryos were cultivated *in vitro* for 3 days. Embryos were evaluated as abnormal, morula or blastocyst. In untreated mice, 90% of fertilized eggs were in late blastocyst stage. Results for LAS were presented in a figure only. The incidence (%) of embryos considered as morula stage was significantly increased (estimated from graph as approximately 35 %) and the percent as blastocyst significantly decreased (estimated as slightly less than 60%). AS was also toxic to embryos. **Possible adverse effect**. Supplemental study. (Kishiyama and Gee, 2/21/03).

008 133941 Same study as 003 126926.

003 126927 Nomura, T., S. Kimura, S. Hata, T. Kanzaki, and H. Tanaka. "The Synthetic Surfactants AS and LAS Interrupt Pregnancy in Mice." (Institute for Cancer Research and Osaka Univ., publ. in *Life Sciences*. 26: 49 - 54 (1980). Linear Alkylbenzene Sulfonate (LAS, no purity stated), 20% aqueous solution, and Alcohol Sulfate (AS) at concentration of 2 or 20%, were applied dermally to female ICR/Jcl mice at several stages of pregnancy. LAS was applied at 0.1 ml, 20%, to a 2 x 3 cm area of "plucked" skin on gestation days 0, 1 and 2, twice daily. Mice were sacrificed on day 3. The oviducts and uterus were removed and the embryos flushed out. After examination, the embryos were cultivated in medium *in vitro*. [See record 003 126926] With LAS, there were 13 pregnant mice with 134 embryos collected. Of these, 21.6% (30/134) were deformed compared to 4.9% (7/143) in the water- treated controls. Normal blastocysts also were lower with LAS being 62/134 (46.3%) compared with 130/143 (91%) in controls. Morulae were 31% with LAS and 4% with water. The conclusion was that LAS [and AS] interrupt pregnancy by a direct effect on the embryos. Data for AS was much more extensive. **Possible adverse effects.** Supplemental study. (Kishiyama and Gee, 2/21/03).

008 133942 Same study as 003 126927.

No record number. Ishii, Y., Y. Samejima, F. Saji and T. Nomura "Effect of alcohol sulfate, linear alkylbenzene sulfonate and natural soap on the development of fertilized eggs of the mouse in vitro." (Osaka Univ., Japan, publ. in *Mutation Res.* 242: 151 - 155 (1990)) Abstract from www.ncbi.nlm…. Eggs from B6 x C3F1 female mice were fertilized in vitro with sperm and treated with synthetic surfactants for 1 hour at the pronucleus stage and cultivated for 5 days. Eggs exposed to LAS (no description) at less than 0.025% developed to the blastocyst stage, as did controls. At greater than 0.03%, no egg developed beyond the 1-cell stage. When LAS was present throughout the 5 days, there appeared to be a threshold between 0.01 and 0.025 %. The conclusion of the authors was that LAS (and AS) can interrupt pregnancy in the mouse by killing the fertilized eggs. (Gee, 3/4/03)

GENE MUTATION

003 126946 Yam, J., K. A. Booman, W. Broddle, L. Geiger, J. E. Heinze, Y. J. Lin, K. McCarthy, S. Reiss, V. Sawin, R. I. Sedlak, R. S. Slesinski and G. A. Wright. (Publ. in *Food Chem. Toxicol.* 22: 761 0 769 (1984)) Review article which included linear alkyl benzene sulfonate as one of the many surfactants. No worksheet. (Gee, 2/24/03).

008 133945 Same as 126946.

003 126899 Inoue, K., T. Sunakawa and S. Takayama. "Studies of *In Vitro* Cell Transformation and Mutagenicity by Surfactants and Other Compounds." (Tochigi Research Laboratories and Department of Experimental Pathology, publ. in *Food Cosmet.Toxicol*. 18: 289 - 296 (1980)) Ten surfactants in the various groups (anionic, cationic, nonionic, amphoteric and other) were tested at various concentrations, with and without metabolic, activation for mutagenic activity using *Salmonella typhimurium* tester strains TA 98 and TA 100. One of those tested was linear alkylbenzene sulfonate (22%). Concentrations used were 0, 10, 25, 50, 100 and 200 µg/plate, with 20 minutes preincubation before plating. The number of plates per concentration was not stated and may have been one. Positive controls were functional. No increase in revertants from the limited data presented. UNACCEPTABLE (major variances including incomplete set of strains, no justification for concentrations, inadequate number of plates). Not upgradeable. (Kishiyama and Gee, 2/14/03).

008 133947 Same study as 003 126899.

CHROMOSOME EFFECTS

003 126896 Hope, J. "Absence of Chromosome Damage in the Bone Marrow of Rats Fed Detergent Actives for 90 Days." (Unilever Research Laboratory, Shanbrook, Bedford (Great Britain), publ in Mutation Research 56: 47 - 50 (1977)). DOBS 055 (44% active, sodium salt, 10 - 15 carbons) was fed at the MTD of 1.13% active and at half the MTD of 0.56% to 6 Wistar rats/sex /group for 90 days. Three other detergents were also tested in the study. Six slides per animal were prepared for scoring. No clastogenic effect was reported for the four detergents. UNACCEPTABLE (insufficient information including no analysis of the diet, no individual data, no justification of doses, others - see worksheet). Upgrade may be possible. (Kishiyama and

Gee, 2/14/03).

008 133946: Same study as 003 126896.

003 126905 Koizumi, N., R. Ninomiya, Y. Inoue, T. Tsukamoto, M. Fujii, and Y. Yamamoto. "Implantation Disturbance Studies with Linear Alkylbenzene Sulphonate in Mice." (Hyogo College of Medicine and Food Chemistry Division, Ministry of Health and Welfare, Japan, Publ. in *Archives Environmental Contamination and Toxicology* 14: 73 - 81 (1985)). Linear alkylbenzene sulfonate (LAS) was administered at to ICR female mice in several experiments. In experiment 1, for preimplantation lose, doses were 0, 14, 70 or 350 mg/kg by oral gavage, either on day 3 as a single dose or on days 1 - 3 of gestation, with 30+ per group. In experiment 2, for distribution in tissues, a dose of 350 mg/kg on day 3 and the animals (10) were sacrificed at 4 or 8 hours. Distribution was determined by HPLC quantitation. In experiment three, mice were given 2 mg/mouse on day 3 (approximately 70 mg/kg) and sacrificed on day 18 for analysis of polychromatic erythrocytes of were given subcutaneous injection of 0, 1, 2, and 10 mg/mouse on day 17. Bone marrow was evaluated on day 19 for effects on maternal bone marrow and fetal liver and blood cells. No treatment related effects were reported on implantation, live fetuses per litter or fetal weight in experiment 1. In mice treated on day 3, distribution at 4 hours was primarily in the stomach/intestine, liver and blood. At 8 hours, the amount in the liver had increased over 4 hours, material was found in the kidney (urinary excretion), blood level increased and stomach/intestine decreased. There was no increased in micronucleated polychromatic erythrocytes by either dosing regimen - oral on day 3 (2 mg/mouse) or subcutaneous on day 17 of gestation. No adverse effects. Supplemental study. (Kishiyama and Gee, 2/14/03) .

DNA DAMAGE

003 126899 [A] Inoue, K., T. Sunakawa and S. Takayama. "Studies of *In Vitro* Cell Transformation and Mutagenicity by Surfactants and Other Compounds." (Tochigi Research Laboratories, Publ. in *Food Cosmet. Toxicol.* 18: 289 - 296 (1980)) Ten surfactants in the various groups (anionic, cationic, nonionic, amphoteric and other) were tested at various concentrations using Syrian golden hamster embryo cells. Linear alkylbenzene sulfonate (22.2% active) was tested at 0, 0.5, 1, 5, 10, 20 or 50 μg/ml with two strains of hamster embryo cells, with activation only. The positive control (3-Methylcholanthrene) was functional. UNACCEPTABLE (major variances). No adverse effect. Not upgradeable (no activation) (Kishiyama and Gee, 2/14/03).

008 133947 Same as 126899.

OTHER

50447 - 003 126873 Antal, M. "Changes in blood glucose level induced by sodium dodecylbenzene sulfonate (SDBS) in rats." (Publ. in *Zeitschrift fur Ernahrungswissenschaft* 12: 144 - 151 (1973)) Groups of 40 male and 50 female albino rats, 160 to 180 g, were fed SDBS at 0.25 g/kg body weight in the diet for 3 months. At the end of this period, the males and females were subdivided into four groups and given one of the following by gavage: 1) distilled water, 1 ml/100 g body weight; 2) glucose, 0.610 g/ml/100 g body weight; 3) SDBS, 0.094 g/ml/100 g or 4) glucose plus SDBS as in groups 2 and 3. Animals were fasted for 18 hours prior to dosing with glucose. Blood samples were taken from the tail every 30 minutes for 180 minutes and blood

glucose determined by the orthotoluidine method. Results: No difference in body weight was noted after 3 months of feeding SDBS. In males, those pretreated with SDBS and controls showed similar responses to glucose loading and SDBS + glucose with blood glucose levels peaking earlier when detergent was given with the glucose loading. With females, the individual data were graphed and there was considerable scatter in both control and SDBS pretreated groups. The author concluded that female rats were more sensitive to detergents. No worksheet. Supplemental study. (Gee, 2/10/03).

007 133864 Same as 126873.

003 126876 Cashner, F., M. Schuyler, R. Fletcher, H. Ritz and J. Salvaggio "Immunologic responses of Cynomolgus monkeys after repeated inhalation exposures to enzyme and enzyme-detergent mixtures." (Tulane University and Proctor and Gamble, publ. in *Toxicology and Applied Pharmacology* 52: 62 - 68 (1980)) Sera were obtained from monkeys used in an inhalation study (see Coate, W. B. *et al.* publ. in *Toxicol. Appl. Pharmacol*. 45: 477-496 (1978). Sera were examined for the presence of enzyme-specific IgE and precipitating antibodies. Lung sections were examined by immunofluorescence for immunoglobulins, complement and fibrinogen. No IgE was found but precipitating antibodies were found in monkeys exposed to enzymes (Alcalase and Milezyme 8X) and potentiated in enzyme-detergent mixtures. No deposits were found in the lungs. Poor copy. Supplemental study. (Gee, 2/10/03).

003 126879 Cresswell, D. G., G. A. Baldock, L. F. Chasseaud and D. R. Hawkins "Toxicology studies of linear alkylbenzene sulphonate (LAS) in rhesus monkeys. II. The disposition of [C^{14}]LAS after oral or subcutaneous administration." (Huntingdon Research Centre, UK, publ. in *Toxicology* 11: 5 - 17 (1978)) Sodium alkyl[C14]benzenesulfonate, radiochemical purity > 99%, in aqueous solution, was used. Groups of 2/sex adult rhesus monkeys were used. For excretion studies, animals were given a single oral gavage dose of 30 mg/kg. For plasma levels, the same animals were given 150 and 300 mg/kg, 2-3 weeks apart. After 2-3 additional weeks, these animals were given daily doses of 30 mg/kg for 7 days. For excretion, urine was collected for 0 - 8 hours, 8 - 24 hours, and 24 hour intervals for another 4 days. Feces were collected at 24 hour intervals. Blood was sampled at 30, 48, 72 and 96 hours. For plasma, blood samples were taken at predosing, 0.5, 1, 2, 4, 6, 7.5 and 24 hours and at 24 hour intervals until radioactivity was at the limit of detection. For repeated doses, blood was sampled at similar intervals after the first dose and before giving the next 6 doses. Single animals given repeat doses were sacrificed at 2, 4, 24 and 48 hours and selected tissues collected. RESULTS: In the first 24 hours after the single dose of 30 mg/kg, 66.5% (males) and 72.1% (females) was excreted in the urine and 14.9 % (M) and 12.7 % (F) in the feces. Total recovery was approximately 100% in 120 hours. After both 150 and 300 mg/kg single dose, plasma concentrations peaked at 4 hours at 41.2 μg/ml and 36.3 μg/ml, respectively. Half lives were approximately 5 - 6.5 hours, depending on dosing regimen. After a single subcutaneous injection, excretion was primarily in the urine and most excreted in the first 48 hours. Some excretion was seen in the feces and was probably due to elimination in bile. Plasma levels peaked at 2 - 4 hours. After multiple oral doses, most of the radioactivity was associated with the stomach, intestinal tract and kidneys at 2, 4 and 24 hours. Concentrations in most other tissues were lower than plasma, indicating no specific accumulation. Analysis of metabolites indicated five main components, which were not conjugates, and all more polar than LAS. Supplemental study. No worksheet. (Gee, 2/11/03).

007 133909 Duplicate of 126879.

003 126892 Drotman, R. B. "Metabolism of cutaneously applied surfactants." (Proctor and Gamble, publ. in *Cutaneous Toxicity*, Academic Press, V. A. Drill and P. Lazar, eds., pages 95 - 109, 1977) ^{35}S-labeled linear alkylbenzene sulfonate (anionic surfactant) was applied to the skin of rats, rabbits, guinea pigs and 2 humans. It remained in contact with animal skin for 72 hours and human skin for 144 hours. The percent of applied dose in urine, feces, CO_2 and skin (or skin wipes) was determined. Most of the applied dose was recovered from the skin in all test subjects. Only traces were found in urine and feces. In humans, the total recovered was 51 and 41% of the applied dose because the skin itself could not be recovered for analysis. The conclusion was that LAS did not effectively penetrate the skin. Supplemental study. No worksheet. (Gee, 2/11/03)

003 126894 Gloxhuber, Ch. "Toxicological properties of surfactants." (Henkel & Cie GmbH, publ. in *Arch. Toxicol.* 32: 245 - 270 (1974) Alkylbenzene sulfonate was one of a number of surfactants discussed. Not reviewed. (Gee, 2/11/03)

003 126895 Heywood, R., R. W. James and R. J. Sortwell " Toxicology studies of linear alkylbenzene sulphonate (LAS) in rhesus monkeys. I. Simultaneous oral and subcutaneous administration for 28 days." (Huntingdon Research Centre, UK, publ. in *Toxicology* 11: 245 - 250 (1978)) Linear alkylbenzene sulfonate (20.5% ai, 78.7% moisture, alkyl chains of 10 to 13 carbons) was used to treat rhesus monkeys, aged 18 - 36 months. They were divided into 4 groups of 3/sex. Doses given by oral gavage were 0 (water), 30, 150 or 300 mg/kg and by subcutaneous injection, 0 (sterile saline), 0.1, 0.5 and 1.0 mg/kg, for 28 days. The combinations were by increasing dose with each route. Hematology, limited clinical chemistry and urinalysis were performed. At termination, a list of organs were weighed and tissues preserved, including the injection site. All monkeys receiving 300 mg/kg and 1.0 mg/kg s.c. vomited on multiple occasions. Passage of loose stools was increased at 150 mg/kg:0.5 mg/kg and higher. There was a dose-related increase in the incidence of chronic inflammation at the injection site with 0/6, 3/6, 5/6 and 6/6 showing the effect. There were no other findings. Apparent systemic NOEL = 30 mg/kg oral and 0.1 mg/kg s.c. with no NOEL for local effects at the injection site. Supplemental study. No worksheet. (Gee, 2/11/03)

007 133910 Same as 126895.

003 126898 Howes, D. "The percutaneous absorption of some anionic surfactants." (Unilever, publ. in *J. Soc. Cosmet. Chem.* 26: 47 - 63 (1975)) Sodium *p*-1-[^{14}C]dodecylbenzene sulfonate (DOBS), 8.5 μCi/mg, was prepared as a 3 mM solution in 25% v/v polyethylene glycol 400 or 3 mM in water. <u>In vitro</u>: penetration through rat and human skin was determined over 24 hours for rats and 48 hours for human (from female abdominal skin at autopsy) with samplings made periodically. For rats, < 0.1 μg/cm^3 penetrated, 30% could be rinsed off and 70% remained with the skin. For humans, < 0.1 μg/cm^3 penetrated in 48 hours, with 30 - 50% remaining with the skin after rinsing (no data). <u>In vivo:</u> Female Colworth-Wistar rats were used with several routes of exposure. Three rats were given intraperitoneal injections and three given subcutaneous injections of 0.1 or 0.5 ml and placed in metabolism cages. After 6 or 24 hours, animals were sacrificed and carcasses homogenized. Excretion rates were the same after either route of injection. Most (78%) was excreted in the urine at 24 hours with 22% remaining in the carcass. <u>Topical application</u>: 0.2 ml was applied to the clipped skin, 3 animals per group. After 15 minutes, the skin was rinsed and the rinsate collected. The treatment site was covered and the animals placed in metabolism cages and monitored for 24 hours. The effect of prewashing the skin was also determined by washing the skin with a mixture of detergents used in the study, at 60 mM each. Animals were then treated as before. Treated site of skin was examined for location of radioactivity. Autoradiography showed heavy deposition on skin surface and upper regions of

hair follicles. No radioactivity was detected in the excreta. Supplemental study. No worksheet. (Gee, 2/14/03)

003 126903 Kirk-Othmer "Encyclopedia of Chemical Technology." 3rd edition, pages 349 - 351 and 1 - 38, John Wiley and Sons, NY, 1983. Discusses primarily the chemistry and manufacturing of a variety of surfactants. Not reviewed. (Gee, 2/14/03).

003 126906 Lin, Y. and S. J. DeSalva "Effects of surfactants on absorption, distribution and excretion of linear alkylbenzene sulfonates in rats." (Colgate-Palmolive, abstract in *Federation Proceedings* 40: 636 (1981)) Male Sprague-Dawley rats were given a single oral dose of 100 mg/kg of LAS alone or in combination with alcohol ethoxysulfate (AEOS) or AEOS plus lauric/myristic monoethanol amide/sodium xylene sulfate. With LAS alone, the mean peak blood level was 13.0 µg/ml at 2.3 hours. The urine excreted 45% and the feces, 45%. At 72 hours, no significant retention was found in 15 selected tissues and organs (not listed). Supplemental study. No worksheet. (Gee, 2/18/03)

003 126907 Markham, R. J. F. and B. N. Wilkie "Effect of detergent on protease-induced mortality and pulmonary histopathology." (University of Guelph, publ. in *Arch. Environmental Health* 34: 418 - 423 (1979)) The detergent used was 40% w/w sodium dodecylbenzene sulfonate and the protease was subtilopeptidase A from *B. subtilis*. Female Hartley strain guinea pigs were exposed to enzyme without and with detergent. Mortality was assessed and lung tissues examined. Detergent alone caused no deaths in fifty animals given a 30 minute exposure, 1% w/v. Lung effects were rated as "mild". No worksheet. (Gee, 2/18/03)

007 133839 Dupl. Of 126907.

003 126912 Michael, W. R. "Metabolism of linear alkylate sulfonate and alkyl benzene sulfonate in albino rats." (Proctor and Gamble, publ. in *Toxicol. Appl. Pharmacol.* 12:473 - 485 (1968)) $LA^{35}S$, 10 - 14 carbons with 11, 12, and 13 predominating, was given orally to fasted male rats (Charles River) in a volume of 1.0 ml. Doses were 0.6, 1.2, 8 or 40 mg/rat. Urine and feces were collected periodically over 3 days. Some rats were bile duct-ligated and given a dose of 1.2 mg. Enterohepatic circulation was quantified by giving a dose of 1.2 mg of rat A with a cannula inserted in the proximal end of the bile duct and the distal end in the bile duct of rat B, so the bile could flow from rat A to rat B. Urine and feces were collected over 90 hours. LAS was readily absorbed from the GI tract with more excreted in the urine than the feces. Little radioactivity was retained in the carcass after 72 hours. In bile duct ligated animals, most of the radioactivity was excreted in the urine. In the dual experiment, the LAS excreted in the bile of rat A was completely absorbed by rat B and excreted in the urine and bile with none in the feces. Some attempts to identify the metabolites were included and found to be a mixture of sulfophenyl butanoic and sulfophenyl pentanoic acids. Supplemental study. No worksheet. (Gee, 2/19/03),

003 126931 Selmeci-Antal, M. and A. Blaskovits "The effect of sodium dodecylbenzene sulphonate (SDBS) and various diets on rat liver glucose-6-phosphatase (G6P-ase) and glucose-6-phosphate dehydrogenase (G6PDH) activities." (Institute of Nutrition, Budapest, publ. in *Nutr. Metab.* 21 (suppl. 1): 244 - 246 (1977)) Male rats, fasted for 3 days, were fed three types of diets containing 0, 6 or 20% sunflower oil. Each of these diets contained 0, 250 or 2500 mg SDBS per kg of diet. SDBS did not influence the serum total lipid or free fatty acid. It did lower the G6PDH activity in the liver at both concentrations in the diet with 20% oil and at the higher concentration in diet with 6% oil. There was no effect in oil-free diet. SUPPLEMENTAL study. No worksheet. (Gee, 2/21/03)

003 126943 Tomiyama, S. "Fundamental study of biochemical behavior of anionic sulfonate- and sulfate-type surfactants." (Lion Fat & Oil Co., Ltd, Japan, publ. in *J. Am. Oil Chemists Soc.* 52: 135 - 138 (1975)) Linear alkylate sulfonate adsorption to human skin was studied with several post-treatment washes. Adsorption to hog bristles and human hair were also studied. No worksheet. Supplemental study. (Gee, 2/24/03).

007 133862 Kimura, T. and A. Yoshida "Toxicity of detergent feeding and effect of the concurrent feeding of dietary fiber in rats." (Nagoya University, Japan, publ. in *Nutrition Reports International* 26: 271 - 279 (1982)) Sodium laurylbenzene sulfonate was one of the detergents used to feed fasted rats for 4 days. At termination, the morphology and histology of the intestinal brush border was evaluated and the level of sucrase activity determined. Not reviewed in detail. No worksheet. (Gee, 2/24/03).

008 133948 Kimura, T., H. Imamura, K. Hasegawa and A. Yoshida "Mechanisms of toxicities of some detergents added to a diet and of the ameliorating effect of dietary fiber in the rat." (Nagoya University, Japan, publ. in *J. Nutr. Sci. Vitaminol.* 28: 483 - 489 (1982)) Male Wistar rats were fasted overnight. A proximal jejunal segment was perfused with Ringer bicarbonate solution (RBS) and the release of enzymes monitored for 150 minutes. Enzymes included sucrase, alkaline phosphatase and maltase. The rate became constant after 30 minutes, corresponding to physiological cell desquamation (page 485). To study the effect of detergents, the jejunum was perfused with RBS for 60 minutes followed by perfusion of the detergent and fiber for 90 minutes. Release of enzymes was monitored. One of the detergents was sodium laurylbenzene sulfonate at 0.5 % using alkaline phosphatase release. The level of release reached 3 to 4 times that of RBS. The results indicated a high exfoliating or releasing effect on the brush border membranes. Supplemental study. No worksheet. (Gee, 2/25/03)

CITATIONS ONLY, NOT SUBMITTED, NOT REVIEWED

Watari, N., K. Torizawa, M. Kanai and Y. Suzuki "Ultrastructural observations of the protective effect of glycyrrhizin for mouse liver injury caused by oral administration of detergent ingredient (LAS)." (publ. in *Electron Microscopy* 10: 121 - 139 (1977)) DDY-strain mice were given 100 ppm DDBSA (≅ 25 mg/kg/day) for 6 months in drinking water and terminated at 1, 2, 3, 6, or 8 months. Ultrastructure studies showed that even at 1 month, treatment-related liver effects were seen. Recovery was noted at 8 months, 2 months after cessation of exposure. (Gee, 2/27/03)

Ito, R., H. Kawamura, H. S. Chang, K. Kudo, S. Kajiwara, S. Toida, Y. Seki, M. Hashimoto and A. Fukushima "Acute, subactue and chronic toxicity of magnesium linear alkylbenzene sulfonate (LAS-Mg)." (publ. in *Toho Igakkai Zasshi* 25: 850 - 875 (1978)) Mg-DDBSA was given orally to 20 Sprague-Dawley rats per sex at 0, 75, 150 or 300 mg/kg/day for 6 months. Summary states that body weight gain was suppressed and some clinical chemistry parameters were decreased but within normal ranges. NOEL given as < 70 mg/kg/day, apparently based on weight. Twelve rats/sex were given oral doses of 0, 155, 310 or 620 mg/kg/day for 1 month. Liver weights were increased at 620 mg/kg and 2 females and 1 male died. Weight gain and food efficiency were lower at all doses. (Gee, 2/27/03)